

AMENDMENTS TO THE CLAIMS

Listing of Claims:

(Cancelled) Claims 1 – 79

80. (Previously Presented) A bidentate motif capable of binding a cytoplasmic protein and activating cellular activities in a cell, said bidentate motif comprising a tyrosine and a serine/threonine residue which are capable of interaction with cytoplasmic proteins, and wherein the residue and cytoplasmic protein can interact to activate cellular activity in the cell.

81. (Previously Presented) A bidentate motif according to claim 80 wherein the tyrosine and serine/threonine residue comprises a binary switch for independent regulation of cellular activity.

82. (Currently Amended) A bidentate motif capable of binding to a cytoplasmic protein according to claim 80 comprising a tyrosine and a serine/threonine residue, said motif comprising an amino acid sequence alignment selected from the group consisting of:

$$N-X-X-\underline{Y}-(X)_{1-13}-[R/K/H/Q]-[X/\psi]_{2-3}-\underline{S/T}-X-P \quad \textbf{(SEQ ID NO: 71)}$$

wherein X is any residue, Y is tyrosine, ~~S/T~~S/T is serine or threonine and ψ is a ~~hydrophilic~~hydrophobic residue or an equivalent thereof; or

$$\underline{Y}-(X)_{1-16}-[R/K/H/Q]-[X/\psi]_{2-3}-\underline{S/T}-X-P \quad \textbf{(SEQ ID NO: 72)}$$

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and ψ is a ~~hydrophilic~~hydrophobic residue or an equivalent thereof; or

$$N-X-X-\underline{Y}-[X]_{1-30}-[R/K/Q'H]-[X]_{1-4}-[\underline{S/T}]-X-p \quad \textbf{(SEQ ID NO: 73)}$$

wherein X is any residue, Y is phosphotyrosine, S/T is phosphoserine/~~phosphothreonine~~
phosphothreonine.

83. (Previously Presented) A bidentate motif according to claim 80 wherein the motif is derived from a receptor.

84. (Previously Presented) A bidentate motif according to claim 80 wherein the motif is derived from the common beta chain (β c).

85. (Previously Presented) A bidentate motif according to claim 80 wherein the tyrosine is equivalent to Tyr577 of the common beta chain (β c) and/or the serine is equivalent to Ser 585 of the common beta chain (β c).

86. (Previously Presented) A bidentate motif according to claim 80 wherein the tyrosine or serine/threonine are independently phosphorylated in response to a cytokine, and phosphorylation is dependent on the cytokine concentration.

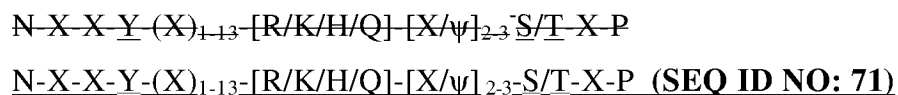
87. (Previously Presented) A bidentate motif according to claim 80 wherein phosphorylation of the serine independently of the tyrosine regulates cell survival.

88. (Previously Presented) A bidentate motif according to claim 80 wherein phosphorylation of the tyrosine independent of the serine regulates cell survival and proliferation.

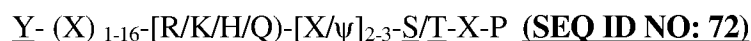
89. (Previously Presented) A bidentate motif according to claim 83, with a modification at a residue equivalent to the Tyr 577 and/or Ser585.

90. (Previously Presented) The bidentate motif according to claim 89 wherein the residue equivalent to Tyr 577 is substituted with phenylalanine and/or the Ser 585 residue is substituted with glycine.

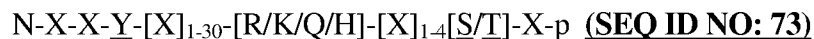
91. (Currently Amended) A method of modulating cellular activity in a cell, said method comprising: modulating phosphorylation of a tyrosine and/or serine residue of a bidentate motif capable of binding to a cytoplasmic protein comprising a tyrosine and a serine/threonine residue, said motif comprising an amino acid sequence alignment selected from the group consisting of:



wherein X is any residue, Y is tyrosine, S/T is serine or threonine and ψ is a ~~hydrophibic~~hydrophobic residue or an equivalent thereof; or



wherein X is any residue, Y is tyrosine, S/T is serine or threonine and ψ is a ~~hydrophibic~~hydrophobic residue or an equivalent thereof; or



wherein X is any residue, Y is phosphotyrosine, S/T is phosphoserine/phosphothreonine.

92. (Previously Presented) A method according to claim 91 wherein the phosphorylation is modulated by mutating the tyrosine and/or serine.

93. (Currently Amended) A method according to claim 92 wherein the ~~Tyr~~tyrosine is substituted for phenylalanine and/or the serine is substituted for glycine.

94. (Previously Presented) A method according to claim 91 wherein the phosphorylation is decreased by subjecting the cell to an antagonist or kinase inhibitor which inhibits phosphorylation of the tyrosine and/or serine.

95. (Currently Amended) A method according to claim 91 wherein cellular activity is inhibited, said method comprising decreasing or inhibiting phosphorylation of the tyrosine ~~and/or~~and/or serine of the bidentate motif.

96. (Previously Presented) A method according to claim 95 wherein the cellular activity is cell survival, said method comprising inhibiting phosphorylation of the serine.

97. (Previously Presented) A method according to claim 95 wherein the cellular activity is cell survival, said method comprising inhibiting phosphorylation of the serine equivalent to Ser585 of the common β c.

98. (Previously Presented) A method according to claim 91 wherein cellular activity is activated, said method comprising inducing phosphorylation of the tyrosine and/or serine of the bidentate motif.

99. (Previously Presented) A method according to claim 98 wherein the cellular activity is cell survival, said method comprising increasing phosphorylation of the serine.

100. (Previously Presented) A method according to claim 91 wherein the cellular activity is cell proliferation, said method comprising increasing phosphorylation of the tyrosine.

101. (Currently Amended) A method of treating a cytokine mediated condition, said method comprising:

regulating activation of phosphorylation of a tyrosine and/or serine of a bidentate motif capable of binding to a cytoplasmic protein comprising a tyrosine and a serine/threonine residue, said motif comprising an amino acid sequence alignment selected from the group consisting of:

$$N-X-X-\underline{Y}-(X)_{1-13}-[R/K/H/Q]-[X/\psi]_{2-3}-\underline{S/T}-X-P$$
 (SEQ ID NO: 71)

wherein X is any residue, Y is tyrosine, ~~S/T~~S/T is serine or threonine and ~~T~~ ψ is a ~~hydrophilic~~hydrophobic residue or an equivalent thereof; or

Y-(X)₁₋₁₆-[R/K/H/Q]-[X/ ψ]₂₋₃-[S/T]-X-P **(SEQ ID NO: 72)**

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and ψ is a ~~hydrophilic~~hydrophobic residue or an equivalent thereof; or

N-X-X-Y-[X]₁₋₃₀-[R/K/Q/H]-[X]₁₋₄-[S/T]-X-p **(SEQ ID NO: 73)**

wherein X is any residue, Y is phosphotyrosine, S/T is phosphoserine/phosphothreonine.

102. (Previously Presented) A method according to claim 101 wherein the cytokine mediated condition is treated by increasing or decreasing activation of phosphorylation of the tyrosine and/or serine of the bidentate motif.

103. (Previously Presented) A method according to claim 101 wherein the phosphorylation is decreased by mutating the tyrosine and/or serine.

104. (Previously Presented) A method use according to claim 103 wherein the motif is mutated by substituting tyrosine for phenylalanine and/or substituting serine for glycine.

105. (Previously Presented) A method according to claim 101 wherein the phosphorylation is decreased by subjecting the cell to an antagonist which inhibits phosphorylation of the tyrosine and/or serine.

106. (Previously Presented) A method according to claim 101 wherein the cytokine mediated condition is a GM-CSF mediated condition.

107. (Previously Presented) A method according to claim 101 wherein the cytokine mediated condition involves cell survival.

108. (Previously Presented) A method according to claim 101 wherein the cytokine mediated condition involves cell proliferation.

109. (Previously Presented) A method according to claim 101 wherein the cytokine mediated condition is selected from the group consisting of myeloid cell activation, asthma and rheumatoid arthritis.

110. (Currently Amended) A method for diagnosing a proliferative condition involving cell proliferation or cell survival, said method including:

detecting a level of phosphorylation of tyrosine and/or serine in a bidentate motif capable of binding to a cytoplasmic protein comprising a tyrosine and a serine/threonine residue, said motif comprising an amino acid sequence alignment selected from the group consisting of:

$$\text{N-X-X-}\underline{\text{Y}}\text{-(X)}_{1-13}\text{-[R/K/H/Q]-[X/}\psi\text{]}_{2-3}\text{-}\underline{\text{S/T}}\text{-X-P } \underline{\text{(SEQ ID NO: 71)}}$$

wherein X is any residue, Y is tyrosine, ~~S/T~~S/T is serine or threonine and ~~T~~ψ is a ~~hydrophilic~~hydrophobic residue or an equivalent thereof; or

$$\underline{\text{Y}}\text{-(X)}_{1-16}\text{-[R/K/H/Q]-[X/}\psi\text{]}_{2-3}\text{-}\underline{\text{S/T}}\text{-X-P } \underline{\text{(SEQ ID NO: 72)}}$$

wherein X is any residue, Y is tyrosine, S/T is serine or threonine and ψ is a ~~hydrophilic~~hydrophobic residue or an equivalent thereof; or

$$\text{N-X-X-}\underline{\text{Y}}\text{-[X]}_{1-30}\text{-[R/K/Q/H]-[X]}_{1-4}\text{-}\underline{\text{[S/T]}}\text{-X-p } \underline{\text{(SEQ ID NO: 73)}}$$

wherein X is any residue, Y is phosphotyrosine, S/T is phosphoserine/phosphothreonine; and

comparing against a cell of a normal level of phosphorylation.